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ARTERIOSCLEROSIS RESEARCH LABORATORY
St. Barnabas Hospital Research Foundation and the
University of Minnesota School of Medicine
601 Tenth Avenue South
Minneapolis 4, Minnesota

December 16, 1964

Dr. Michael De Bakey
Department of Surgery
Baylor University School of Medicine
Houston 25, Texas

Dear Dr. De Bakey:

I hesitate to add to your burden in the collection of data as Head of the Presidential Commission on Heart Disease, Cancer, and the Stroke. I will therefore discuss only briefly that which, in my judgement, is the most important and yet a neglected area in the nations effort to reduce the death toll from heart disease and the stroke. This area is our inability to accurately evaluate the individual with regard to a biochemical index of the activity level of atherogenic factors. From this statement it becomes evident that the problem revolves around learning the cause of arteriosclerosis. It is in this area where the scientific community has become bogged down by individuals and groups fighting for the financial support of their own important but limited research project; the consequence thereof being unjust criticism of pertinent variables in someone elses laboratory and hence prejudice and confusion with little forward movement.

However, at this time there are a significant number of enzymatic activities and specific protein and non-protein factors which have been statistically correlated with arteriosclerosis. For just one example, in my laboratory we have found that the turnover rate of fibrinogen increases 45.4 %, as a function of age, in the 53 yr old subject. If subjects of this age group incur an infarct, the turnover rate will increase by 79.2 % above the young normal subject. Both increases above the young normal subject are significant at $P < 0.001$. The increase of the arteriosclerotic subject with respect to the age matched normal is significant at $P < 0.04$. These increases are not a function of anticoagulant therapy or the stress or trauma of the myocardial infarct.

Although, we have at this time a number of biochemical indices of atherogenesis, the problem is that no one has the physical facility and staff which would permit an adequate evaluation of the degree of correlation between activity or concentration levels of these factors and the degree of arteriosclerosis in the living and deceased subject. I believe that such a broadly conceived study is not only feasible at this time but is an integral part of the fight against vascular disease and thus will be essential sooner or later. It is possible that an adequate statistical study of the known factors which change as a function of arteriosclerosis would allow a regional center to take any individual and by measuring these biochemical activities be able to predict an infarct within a matter of a few weeks or days. While this may be of limited

value, the more important development would be the availability of facilities and staff for determining the effect of therapy on the change in these biochemical indices and on the physical indices of the progress or regression of arteriosclerosis. With respect to therapy, facilities and staff would be available for basic studies of intracellular and extracellular control mechanisms which may change as a function of vascular disease, changes which may be located at such fundamental levels as the transcription of DNA, translation of the RNA message, and protein and enzyme synthesis.

Suffice it to say that this is a very rough and incomplete outline of probably the most pressing problem in the area of heart disease and the stroke. It is evident that the answers must come from the biochemical or molecular or enzymatic level. The Framingham Heart Study might be considered as a guide of that which needs to be done at the molecular level and of that which needs to be done at a greatly increased level of sensitivity and specificity.

I find it doubtful that such a study emanating from one group, such as my own, could secure adequate support through the NIH Study Section System. However, an approach through direct financing by NIH, such as their recent multi-million dollar program on viruses, would appear workable. Or an approach or proposal emanating from 5 or 6 regional principle investigators and their co-workers might be able to receive approval through the Study Section System.

I am most interested in pursuing further this line of thought and wish to learn your thoughts, your recommendations, and whether any action on this matter might be facilitated by or forthcoming via the efforts of your commission.

With my kindest regards, I am,

Sincerely yours,

L. O. Pilgeram

Laurence O. Pilgeram, Ph. D.
Director

via air mail
LOP:cz